## **AMENDMENTS TO THE CLAIMS**

The following <u>Listing of the Claims</u> will replace all prior versions and all prior listings of the claims in the present application:

1.(Currently Amended) A computer program product comprising:

a computer readable medium having computer readable program code embodied in the medium for causing an application program to execute on a computer,

wherein the program product comprises instructions for controlling one or more functions of a microfluidic substrate in response to received data regarding one or more substrate properties, wherein the one or more functions comprises sequentially exposing a cell based biosensor in electrical communication with an electrode to multiple fluid streams from one or more microchannels in the substrate by moving the sensor, moving the substrate, moving both the sensor and the substrate and/or by varying pressure of one or more of the microchannels.

 (Currently Amended) A computer program product comprising a computer readable medium having computer readable program code embodied in the medium for causing an application program to execute on a computer,

wherein the program product comprises instructions for controlling one or more functions of a microfluidic substrate in response to received data regarding one or more properties of a sensor in fluid communication with at least one microchannel of the substrate and optionally, for controlling one or more functions of the microfluidic substrate in response to received data regarding one or more substrate properties and, wherein the one or more functions comprises sequentially exposing a cell based biosensor in electrical communication with an electrode to multiple fluid streams from one or more microchannels in the substrate by moving the sensor, moving the substrate, moving both the sensor and the substrate and/or by varying pressure of the one or more of the microchannels.

- (Currently Amended) A computer program product comprising a computer readable medium having computer readable program code embodied in the medium for causing an application program to execute on a computer,
  - wherein the program product comprises instructions for controlling one or more functions of a microfluidic substrate, including instructions for controlling the exposure of a cell based biosensor to multiple fluid streams from scanning of a sensor relative to a plurality of outlets of one or more microchannels in the substrate by varying the pressure of one or more of the microchannels.
- 4. (Cancelled)
- 5. (Cancelled)
- 6. (Cancelled)
- 7. (Currently Amended) The computer program product of elaim 5any of claims 1 3, wherein scanning is interrupted by one or more programmed pauses during a selected time interval.
- 8. (Currently Amended) The computer program product of any of claims 1 3, wherein the one or more functions <u>further comprises a function</u> is selected from the group consisting of: the movement of fluid in at least one microfluidic channel of the substrate; the movement of a cell in at least one microfluidic channel of the substrate; the delivery of an agent to at least one channel in the substrate; the movement of an agent in at least one channel in the substrate; scanning a sensor relative to an outlet of at least one microchannel in the substrate by moving the sensor; moving the substrate, moving both the sensor and the substrate; varying pressure in at least one microchannel; separation of molecules and/or ions in at least one channel of the substrate, concentration of molecules in at least one channel of the substrate; mixing; heating; focusing; detection; electroosmosis; electrophoresis; electroporation; electroinjection, electrofusion, recording electrical properties of a sensor in fluid communication with the at least one channel; changes in fluid pressure; and combinations thereof.

- 9. (Original) The computer program code according to claim 8, wherein the one or more functions comprises scanning a sensor relative to an outlet of at least one channel in the substrate and wherein the computer program product comprises a computer readable program code for coordinating scanning with data acquisition.
- 10. (Currently Amended) The computer program product of any of claims 1-3, wherein the computer program product further comprises a computer readable program code for causing a computer to input data received from a detector in proximity to the <u>cell based biosensor</u>.
- 11. (Currently Amended) The computer program product of claim 10, wherein the data comprises signal data relating to a response or reaction of the <u>cell based</u> biosensor.
- 12. (Original) The computer program product of claim 11, wherein the response or reaction is selected from the group consisting of a physiological response, a change in Calcium levels, hybridization, binding, change in electrical properties, introduction of an agent into and/or onto a cell, introduction of an agent into an intracellular compartment, a change in electrical properties of a cell, and combinations thereof.
- 13. (Currently Amended) The computer program product of claim 12, wherein the one or more functions comprises delivering an agent to the <u>cell based bio</u>sensor and wherein the signal data comprises data relating to a response or reaction of the <u>cell based bio</u>sensor to the agent.
- 14. (Currently Amended) The computer program product of any of claims 1-3, wherein the one or more functions <u>further</u> comprises delivering an agent to the <u>cell based biosensor</u>, and wherein the computer program product comprises a computer readable program code for coordinating delivery of the agent with data acquisition.

- 15. (Original) The computer program product of any of claims 1-3, wherein the microfluidic substrate further comprises at least one reservoir and/or cell chamber in communication with at least one channel of the substrate.
- 16. (Currently Amended) The computer program product of claim 15\_wherein the one or more functions <u>further</u> comprises delivery of a fluid and/or agent from the channel to the reservoir and/or cell chamber.
- 17. (Currently Amended) The computer program product of claim 15, wherein the one or more functions comprises exposure of the at least one channel, reservoir and/or cell chamber and or a sensor in the at least one channel, reservoir and/or cell chamber to an electric field.
- 18. (Currently Amended) The computer program product of claim 17, and wherein the computer program product comprises a computer readable program code for causing a computer to input data relating to electric field properties.
- 19. (Currently Amended) The computer program product of claim 2 or 3, wherein the one or more functions <u>further</u> comprises delivering an agent to the sensor, and wherein the computer program product comprises a computer readable program code for causing a computer to input data relating to electric field properties and/or a response or reaction to the agent.
- 20. (Currently Amended) The computer program product of any of claims 1-3, wherein the one or more functions <u>further</u> comprises delivering an agent to at least one channel of the substrate and wherein the computer program product comprises a computer readable program code for causing a computer to input data relating a parameter of the agent.
- 21. (Original) The computer program product of claim 20, wherein the parameter is selected from the group consisting of: name of agent, amount of agent; a property of the agent, a previous response of a sensor to the agent, and combinations thereof.

- 22. (Original) The computer program product of claim 20, wherein the agent is delivered from the at least one channel to a sensor and wherein the computer program code further comprises instructions for generating output data relating to the response of a sensor to the agent.
- 23. (Original) The computer program product of claim 22, wherein the output data comprises a dose-response data.
- 24. (Original) The computer program product of any claims of 1-3, wherein the computer program product further comprises instructions for execution by a processor in communication with a fluid delivery control mechanism which controls delivery of fluid through at least one channel of the substrate.
- 25. (Original) The computer program product of claim 24, wherein the fluid delivery control mechanism controls the delivery of streams of buffer and agent through channels of the substrate.
- 26. (Original) The computer program product of claim 24, wherein the fluid delivery control mechanism controls the delivery of fluid streams selected from the group consisting of: streams of different doses of agonists; streams of different doses of antagonists; streams of one or more agonists, streams of one or more antagonists, streams of buffer, and combinations thereof.
- 27. (Original) The computer program product of any of claims 1-3, wherein the computer program product further comprises instructions for execution by a processor in communication with a pressure control mechanism to vary pressure in at least one channel of the substrate.
- 28. (Original) The computer program product of claim 27, further comprising instructions for execution by a processor in communication with an agent delivery control mechanism to deliver of an agent through at least one channel of the substrate.

- 29. (Original) The computer program product of claim 28, wherein the instructions comprise instructions to deliver different agents to at least two channels of the substrate.
- 30. (Original) The computer program product of claim 28, wherein the instructions comprise instructions to deliver different amounts of agents to at least two channels of a substrate.
- 31. (Original) The computer program product of claim 28, wherein the instructions comprise instructions to change an amount of agent delivered to at least one channel of a substrate.
- 32. (Original) The computer program product of claim 28, wherein the instructions comprise instructions to deliver buffer through at least one channel of the substrate.
- 33. (Original) The computer program product of claim 28, wherein the instructions comprise instructions to deliver buffer through a channel adjacent to at least one channel delivering an agent.
- 34. (Original) The computer program product of claim 2 or 3, wherein the computer program product further comprises instructions to superfuse the sensor with buffer at selected time intervals, and wherein the instructions include a providing delay between acquisition of data relating to a response or reaction of the sensor and exposure to the buffer.
- 35. (Withdrawn) The computer program product according to any of claims 1-3, wherein the computer program product further comprises a memory, storing data relating to substrate properties.
- 36. (Original) The computer program product according to claim 2 or 3, wherein the computer program product comprises a memory storing data relating to properties of the sensor.

- 37. (Original) The computer program product of claim 36, wherein the properties of the sensor comprise reactions or responses of the sensor.
- 38. (Original) The computer program product according to any of claims 1-3, wherein the computer program product comprises a memory storing data relating to parameters of functions of the microfluidic substrate.
- 39. (Original) The computer program product of any of claims 1-3, wherein the substrate property is selected from the group consisting of: number of channels in the substrate, channel geometry, distance between channel outlets; distance between channel inlets, position of one or more sensors relative to channel outlets; position of the substrate relative to a scanning device; the position of at least one channel of the substrate; position of a substrate relative to a sensor; substrate material, substrate temperature; and combinations thereof.
- 40. (Currently Amended) The computer program product of any of claims 1-3, wherein the computer program product comprises instructions to alter a parameter of the one or more functions in response to a measured condition of the microfluidic substrate or a sensor in communication with at least one channel of the microfluidic substrate.
- 41. (Original) The computer program product of claim 40, wherein the measured condition is selected from the group consisting of: arrival of an analyte, agent, and/or cell at a channel outlet, arrival of an analyte, agent, and/or cell at a microchannel inlet, fluid movement through the at least one channel, an electroporation event, an electrophoresis event, a concentration event, a separation event, a mixing event, a recording event, pressure, a change in pressure, fluid velocity, a change in fluid velocity, a parameter of an electric field, and combinations thereof.
- 42. (Original) The computer program product of claim 40, wherein the substrate function comprises scanning and the parameter of the function is selected from the group consisting of: the number of microchannel outlets to be scanned, time to

- complete scanning, length of pauses at microchannel outlets, speed of scanning, trajectory of scanning, maximum speed of scanning, alternating channel delay, continuous movement, scanning in response to a selected input received from a sensor, pressure at at least one channel, fluid velocity in at least one channel and combinations thereof.
- 43. (Original) The computer program product of any of claims 1-3, wherein the computer program product further comprises instructions for a processor in communication with a macroscale device which is in communication with the microfluidic substrate.
- 44. (Original) The computer program product of claim 43, wherein the macroscale device is selected from the group consisting of: a power supply, a pump head, pump, degasser, flow meter, injector manifold, a fluid delivery system, an agent delivery system, a pressure sensor; flow cell; concentration manifold, a cartridge, a fitting, a connector, a switch, a valve, a septum, a mixer, a compressor, an ultrasonic bed, an extractor, a focusing device, a dialysis chamber, an absorption chamber, a metabolite chamber, a toxicity chamber, a cell chamber, a detector, an RFID tag, a reagent vessel, a separation column, a focusing column, a size exclusion column, an ion-exchange column; affinity column, a mass spectrometer, a solid-phase extraction bed, a filter, a sieve; a frit, a depth filter, a heater, a heat exchanger, a cooler; a magnetic field generator; electroporation device, electroinjector, microinjector, nanoinjector, a patch clamp pipette, a micropositioner, a micromanupulator, a microscope stage, a signal amplifier, a light source, and combinations thereof.
- 45. (Original) The computer program product of claim 43, wherein the instructions relate to an operation of the macroscale device on the microfluidic substrate.
- 46. (Original) The computer program product of claim 45, wherein the operation comprises delivery of fluid, an agent, a cell, pressure, a voltage, a current, ultrasound, light, and/or a radiofrequency to a region on the substrate.

- 47. (Original) The computer program product of claim 46, wherein the region comprises a channel, a reservoir or a cell chamber.
- 48. (Original) The computer program product of claim 46, wherein the operation comprises separation of molecules or ions in a fluid to be delivered to or from a channel, reservoir or cell chamber in the substrate.
- 49. (Original) The computer program product of claim 48, wherein the molecules or ions are selected from the group consisting of: proteins, polypeptides, peptides, nucleic acids, organic molecules, inorganic molecules, carbohydrates, metabolites, positive ions, negative ions, and combinations thereof.
- 50. (Original) The computer program product of claim 45, wherein the operation comprises heating or cooling of a fluid to be delivered to a channel in the substrate.
- 51. (Original) The computer program product of claim 45, wherein the operation comprises moving the substrate or a component of the substrate.
- 52. (Original) The computer program product of claim 51, wherein the component of the substrate comprises a sensor.
- 53. (Original) The computer program product of claim 45, wherein the operation comprises exposing a region of the substrate to light from a light source, and wherein the light source is a laser in optical communication with a sensor in a channel, reservoir and/or cell chamber of the substrate.
- 54. (Original) The computer program product of any of claims 1-3, wherein the computer program product further comprises computer program code for generating and displaying a graphical user interface.
- 55. (Original) The computer program product of claim 54, wherein the graphical user interface displays a screen on which at least one substrate property, parameter of substrate function, parameter of the macroscale device function, and/or property of a sensor in communication with the substrate, is displayed.

- 56. (Original) The computer program product of claim 54, wherein the graphical user interface displays a screen comprising fields for inputting data relating to the at least one substrate property, parameter of substrate function, parameter of the macroscale device function, and/or property of a sensor in communication with the substrate.
- 57. (Currently Amended) The computer program product of claim 54, wherein the function parameter is selected from the group consisting of the number of microchannel outlets to be scanned, time to complete scanning, length of pauses at microchannel outlets, speed of scanning, maximum speed of scanning, the trajectory of scanning and combinations thereof.
- 58. (Original) The computer program product of claim 57, wherein the trajectory of scanning is linear, non-linear or a combination thereof.
- 59. (Original) The computer program product of claim 54, wherein the graphical user interface displays a screen providing selectable options for a plurality of different scan modes for moving the substrate relative to a sensor, moving a sensor relative to a substrate, and/or varying pressure in at least one microchannel.
- 60. (Original) The computer program product of any of claims 1-3, wherein the computer program product comprises a data acquisition program embedded in a computer readable medium.
- 61. (Original) The computer program product of claim 60, wherein the data acquisition program comprises a search function, a relationship determining function, and/or a data retrieval function.
- 62. (Currently Amended) The computer program product of any of claims 1-3, wherein the computer readable medium further comprises a memory comprising data relating to scanning a sensor across one or more fluid streams of the microfluidic substrate and/or varying pressure at one or more microchannels of the microfluidic substrate.

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- 63. (Original) The computer program product of claim 62, wherein the data relating to scanning the sensor comprises data relating to the number of microchannel outlets scanned, the time to complete a scan, pause time intervals at one or more channels, a property of a fluid stream delivered by one or more microchannel outlets, pressure at one or more microchannels, fluid velocity in one or more microchannels, data relating to the sensor response at one or more microchannel outlets, data relating to the trajectory of scanning and combinations of such data.
- 64. (Original) The computer program product of claim 63, wherein the property of the fluid stream comprises an identity or property of an agent in the fluid stream.
- 65. (Original) The computer program product of claim 2 or 3, wherein the sensor is a cell, a cell fraction, an organelle, a membrane comprising an ion channel, a receptor, a nucleic acid, a protein, a polypeptide, a peptide, small molecule, a drug, a chemical compound, a compound library, gene chip, protein chip, a surface plasmon energy sensor; an FET sensor; an ISFET; an electrochemical sensor; an optical sensor; an acoustic wave sensor; a sensor comprising a sensing element associated with a Quantum Dot particle; a polymer-based sensor; a single molecule or an array of molecules immobilized on a substrate.
- 66. (Original) The computer program product of claim 64, wherein the agent is selected from the group consisting of a drug; irritant; known toxin; candidate toxin; know carcinogen; candidate carcinogen; known mutagen; candidate mutagen; protein; polypeptide; peptide; amino acid; antibody; antigen binding molecules; antigen; hapten; pyrogen; cytokine; growth factor; cell; cell fraction; organelle; secretogogue; virus; viral particle; receptor; a modulator of receptor; ligand; enzyme; enzyme modulator; enzyme substrate; hormone; metabolite; nucleic acid, nucleotide, nucleobase; sugar; carbohydrate, small molecule; metal; ion; and analogs and modified forms thereof.

- 67. (Currently Amended) The computer program product of any of claims 1-3, further comprising instructions for managing, searching, mining, organizing, comparing, and/or representing data.
- 68. (Original) A microfluidic workstation comprising a data acquisition system for executing a computer program product of any of claims 1-3, wherein the data acquisition system is operably linked to the microfluidic substrate.
- 69. (Currently Amended) The workstation of claim 68, wherein the system provides data to a processor in communication with the substrate to alter one or more substrate functions.
- 70. (Original) The workstation of claim 69, wherein the system is pre-programmed to alter one or more substrate functions.
- 71. (Original) The workstation of claim 69, wherein one or more substrate functions is altered in response to feedback from the substrate.
- 72. (Original) The workstation according to claim 69 wherein the one or more substrate functions is selected from the group consisting of: the movement of fluid in at least one microfluidic channel of the substrate; the movement of a cell in at least one microfluidic channel of the substrate; the delivery of an agent to at least one channel in the substrate; the movement of an agent in at least one channel in the substrate; scanning a sensor relative to an outlet of at least one microchannel in the substrate by moving the sensor, moving the substrate, moving both the sensor and the substrate, or by varying pressure at at least one channel of the substrate; separation of molecules and/or ions in at least one channel of the substrate; mixing; heating; focusing; detection; electroosmosis; electrophoresis; electroporation; electroinjection, electrofusion, recording electrical properties of a sensor in fluid communication with the at least one channel; changes in fluid pressure; and combinations thereof.

- 73. (Original) The workstation of claim 68, wherein the workstation comprises a data processing system comprising a memory.
- 74. (Original) The workstation of claim 73, wherein the data processing system accesses data from one or more computer program products, and wherein the data relates to properties or functions of the microfluidic substrate and/or properties of a sensor in fluid communication with at least one channel of the microfluidic substrate.
- 75. (Currently Amended) The workstation of claims 73 or 74 wherein the data processing system accesses data through one or more external databases.
- 76. (Original) The workstation of claim 68, wherein the system further comprises a sensor in fluid communication with at least one channel of the microfluidic substrate.
- 77. (Original) The workstation of claim 68, wherein the substrate comprises an identifier that can identify the substrate to a computer program product for accessing data relating to substrate properties and/or functions.
- 78. (Original) The workstation of claim 68, wherein the workstation further comprises a macroscale device.
- 79. (Original) The workstation of claim 78, wherein the macroscale device is selected from the group consisting of: a power supply, a pump head, pump, degasser, flow meter, injector manifold, a fluid delivery system, an agent delivery system, a pressure sensor; flow cell; concentration manifold, a cartridge, a fitting, a connector, a switch, a valve, a septum, a mixer, a compressor, an ultrasonic bed, an extractor, a focusing device, a dialysis chamber, an absorption chamber, a metabolite chamber, a toxicity chamber, a cell chamber, a detector, an RFID tag, a reagent vessel, a separation column, a focusing column, a size exclusion column, an ion-exchange column; affinity column, a mass spectrometer, a solid-phase extraction bed, a filter, a sieve; a frit, a depth filter, a heater, a heat exchanger, a cooler; a magnetic field generator; electroporation device,

- electroinjector, microinjector, nanoinjector, a patch clamp pipette, a micropositioner, a micromanupulator, a microscope stage, a signal amplifier, a light source, and combinations thereof.
- 80. (Original) The workstation of claim 78, wherein the macroscale device is in communication with a processor that receives instructions from the computer program product.
- 81. (Previously Presented) The workstation of claim 78, wherein the macroscale device comprises a detector for detecting a reaction or response of a sensor exposed to a fluid delivered by the substrate.
- 82. (Original) The workstation of claim 81, wherein the data acquisition system receives input data from the detector relating to the reaction or response.
- 83. (Original) The workstation of claim 82, wherein the input data comprises signal data relating to a response or reaction of the sensor.
- 84. (Original) The workstation of claim 83, wherein the reaction or response is selected from the group consisting of: a physiological response, a change in calcium levels, hybridization, binding, change in electrical properties, introduction of an agent into and/or onto a cell, introduction of an agent into an intracellular compartment, and combinations thereof.
- 85. (Original) The workstation of claim 69, wherein the one or more functions is executed in response to acquisition of data by the data acquisition system.
- 86. (Original) The workstation of claim 82, wherein the data acquisition system performs one or more operations on the data and executes the one or more functions when a predefined result of the one or more operations is obtained.
- 87. (Original) The workstation of claim 69, wherein the microfluidic substrate further comprises at least one reservoir and/or cell chamber in communication with at least one channel of the substrate.

- 88. (Currently Amended) The workstation of claim 69, wherein the one or more functions comprises delivery of a fluid and/or agent from the at least one channel to the reservoir and/or cell chamber.
- 89. (Currently Amended) The workstation of claim 69 or 88, wherein the one or more functions comprises exposure of the at least one channel, reservoir and/or cell chamber and or a sensor in the at least one channel, reservoir and/or cell chamber to an electric field.
- 90. (Original) The workstation of claim 89, wherein the data acquisition system receives input data from the workstation relating to properties of the electric field.
- 91. (Original) The workstation of claim 89, wherein the data acquisition system provides output data to a processor in communication with a power supply for generating the electric field.
- 92. (Original) The workstation of claim 91, wherein the output data comprises instructions for changing one or more properties of the electric field.
- 93. (Currently Amended) The workstation of claim 68, wherein the substrate comprises at least one channel and the workstation further comprises an agent delivery system for delivering one or more agents to at least one channel of the substrate.
- 94. (Original) The workstation of claim 68, wherein the substrate comprises at least one electrically conducting surface for delivering an electric field to a sensor in fluid communication with the at least one channel.
- 95. (Original) The workstation of claim 94, wherein the sensor comprises a cell structure and the electric field is of a strength sufficient to electroporate a membrane of the cell structure.
- 96. (Original) The workstation of claim 95, wherein the computer program product comprises a computer readable program code for causing a computer to input data relating to electric field properties and/or a response or reaction of the sensor to an agent.

- 97. (Original) The workstation of claim 69, wherein the one or more functions comprises delivering an agent to at least one channel of the substrate and wherein the computer program product comprises a computer readable program code for causing a computer to input data relating a parameter of the agent.
- 98. (Original) The workstation of claim 97, wherein the parameter is selected from the group consisting of: name of agent, amount of agent; a property of the agent, a previous response of a sensor to the agent; and combinations thereof.
- 99. (Original) The workstation of claim 97, wherein the agent is delivered from the at least one channel to a sensor and wherein the computer program code further comprises instructions for generating a output data relating to the response of the sensor to the agent.
- 100. (Original) The workstation of claim 68, wherein the workstation further comprises a fluid delivery mechanism for controlling delivery of fluid through at least one channel of the substrate and wherein the computer program code further comprises instructions for execution by a processor in communication with the fluid delivery control mechanism to control delivery of fluid.
- 101. (Original) The workstation of claim 100, wherein the instructions comprise instructions to deliver a plurality of agents to one or more channels of the substrate.
- 102. (Original) The workstation of claim 101, wherein the instructions comprise instructions to deliver different agents to at least two channels of the substrate.
- 103. (Original) The workstation of claim 101, wherein the instructions comprise instructions to deliver different amounts of agents to at least two channels of a substrate.
- 104. (Original) The workstation of claim 100, wherein the instructions comprise instructions to change an amount of agent delivered to at least one channel of a substrate.

- 105. (Original) The workstation of claim 100, wherein the instructions comprise instructions to deliver buffer through at least one channel of the substrate.
- 106. (Original) The workstation of claim 102, wherein the instructions comprise instructions to deliver buffer through a channel adjacent to at least one channel delivering an agent.
- 107. (Original) The workstation of claim 68, wherein the data acquisition system comprises a memory for storing data relating to at least one substrate property.
- 108. (Original) The workstation of claim 68, wherein the data acquisition system comprises a memory for storing data relating to parameters of functions of the microfluidic substrate.
- 109. (Original) The workstation of claim 107, wherein the at least one substrate property is selected from the group consisting of: number of channels in the substrate, channel geometry, distance between channel outlets; distance between channel inlets, position of one or more sensors relative to channel outlets; position of the substrate relative to a scanning device; the position of at least one channel of the substrate; position of a substrate relative to a sensor; substrate material, substrate temperature; and combinations thereof.
- 110. (Original) The workstation of claim 69, wherein the substrate function comprises scanning and the parameter of the function is selected from the group consisting of: the number of microchannel outlets to be scanned, time to complete scanning, length of pauses at microchannel outlets, speed of scanning, maximum speed of scanning, alternating channel delay, continuous movement, scanning in response to a selected input received from a sensor, trajectory of scanning, pressure at at least one microchannel, and combinations thereof.
- 111. (Original) The workstation of claim 68, wherein the computer program product further comprises instructions for a processor in communication with a macroscale device that is in communication with the microfluidic substrate.

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- 112. (Original) The workstation of claim 111, wherein the macroscale device is selected from the group consisting of: a power supply, a pump head, pump, degasser, flow meter, injector manifold, a fluid delivery system, an agent delivery system, a pressure sensor; flow cell; concentration manifold, a cartridge, a fitting, a connector, a switch, a valve, a septum, a mixer, a compressor, an ultrasonic bed, an extractor, a focusing device, a dialysis chamber, an absorption chamber, a metabolite chamber, a toxicity chamber, a cell chamber, a detector, an RFID tag, a reagent vessel, a separation column, a focusing column, a size exclusion column, an ion-exchange column; affinity column, a mass spectrometer, a solid-phase extraction bed, a filter, a sieve; a frit, a depth filter, a heater, a heat exchanger, a cooler; a magnetic field generator; electroporation device, electroinjector, microinjector, nanoinjector, a patch clamp pipette, a micropositioner, a micromanupulator, a microscope stage, a signal amplifier, a light source, and combinations thereof.
- 113. (Original) The workstation of claim 111, wherein the instructions relate to an operation of the macroscale device on the microfluidic substrate.
- 114. (Currently Amended) The workstation of claim 113, wherein the operation comprises delivery of fluid, pressure, a voltage, a current, and/or a radiofrequency to a region on the substrate.
- 115. (Original) The workstation of clam 114, wherein the region comprises a channel, reservoir or cell chamber.
- 116. (Original) The workstation of claim 114, wherein the operation comprises an operation on a fluid to be delivered to a channel, reservoir and/or cell chamber in the substrate.
- 117. (Original) The workstation of claim 116, wherein the operation comprises delivery of fluid, an agent, a cell, pressure, a voltage, a current, ultrasound, light, and /or a radiofrequency to a region on the substrate.

- 118. (Original) The workstation of claim 114, wherein the operation comprises separation of molecules and/or ions in a fluid to be delivered to a microchannel in the substrate.
- 119. (Original) The workstation of claim 118, wherein the molecules and/or ions are selected from the group consisting of proteins, polypeptides, peptides, nucleic acids, organic molecules, inorganic molecules, carbohydrates, metabolites, positive ions, negative ions, and combinations thereof.
- 120. (Original) The workstation of claim 114, wherein the operation comprises heating or cooling of a fluid to be delivered to a channel in the substrate.
- 121. (Original) The workstation of claim 114, wherein the operation comprises moving the substrate or a component of the substrate.
- 122. (Currently Amended) The workstation of claim 121, wherein the component of the substrate comprises a <u>cell based biosensor</u>.
- 123. (Currently Amended) The workstation of claim 122, wherein the sensor comprises a cell or cell fraction.
- 124. (Original) The workstation of claim 114, wherein the operation comprises exposing a region of the substrate to light from a light source.
- 125. (Currently Amended) The workstation of claim 124, wherein the light source is a laser in optical communication with a sensor in a microchannel, reservoir and/or cell chamber of the substrate.
- 126. (Original) The workstation of claim 68, wherein the workstation further comprises a user device for generating and displaying a graphical user interface in response to instructions from the computer program product.
- 127. (Currently Amended) The workstation of claim 126, wherein the graphical user interface displays a screen on which at least one substrate property, property of

- a sensor, parameter of substrate function, and/or parameter of the macroscale device function is displayed.
- 128. (Original) The workstation of claim 126, wherein the graphical user interface displays a screen comprising fields for inputting one or more function parameters.
- 129. (Currently Amended) The workstation of claim 128, wherein the function parameters are selected from the group consisting of: arrival of an analyte, agent, and/or cell at a channel outlet, arrival of an analyte, agent, and/or cell at a microchannel inlet, fluid movement through the at least one channel, an electroporation event, an electrophoresis event, a concentration event, a separation event, a mixing event, a recording event, a scanning event, pressure, a change in pressure, fluid velocity, a change in fluid velocity, a parameter of an electric field, and combinations thereof.
- 130. (Currently Amended) The workstation of claim 129, wherein the graphical user interface displays a screen providing selectable options for a plurality of different scan modes for scanning a sensor relative a substrate, by moving the sensor, the substrate, the substrate and sensor, and/or by varying pressure at least one microchannel of the substrate.
- 131. (Currently Amended) The workstation of claim 68, wherein the data acquisition system comprises a data acquisition program comprising a search function, a data organizing or managing function, a data mining function, a relationship-determining function and/or a data retrieval function.
- 132. (Currently Amended) The workstation of claim 68, wherein the data acquisition system further comprises a memory comprising data relating to scanning a sensor across one or more fluid streams of the microfluidic substrate and/or data relating to pressure changes at at least one microchannel of the microfluidic substrate.

- 133. (Currently Amended) The workstation of claim 132, wherein the data relating to scanning the sensor comprises data relating to the number of microchannel outlets scanned, the time to complete a scan, pause time intervals at one or more channels, a type of fluid stream delivered by one or more microchannel outlets, pressure in one or more microchannels, fluid velocity in one or more microchannels, and data relating to the sensor response at one or more microchannel outlets.
- 134. (Currently Amended) The workstation of claim 68, wherein the workstation further comprises a stage for receiving the substrate which can be moved in one or more of an x-, y-, or z- direction and/or by rotating and/or by tilting.
- 135. (Original) The workstation of claim 68, wherein the workstation further comprises a computer program product for patch clamp data acquisition and analysis.
- 136. (Original) The workstation of claim 134, further comprising one or more mechanisms for controlling the movement of the stage.
- 137. (Original) The workstation of claim 136, wherein the one or more mechanisms comprises one or more joysticks.
- 138. (Original) The workstation of claim 126, wherein the graphical user interface displays a representation of the substrate on a screen of the user interface.
- 139. (Original) The workstations of claim 138, wherein coordinates of the representation are selected and in response to the selecting, an operation at corresponding coordinates on the substrate occurs.
- 140. (Original) A suite of computer program products comprising a computer program product according to any of claims 1-3 and a data acquisition program for patch clamp data acquisition.
- 141. (Original) The suite of computer program products according to claim 140 wherein the data acquisition program comprises computer program code for analyzing patch clamp data.

## 142. (Original) A system comprising:

- a first computer program product according to any of claims 1-3;
- a second computer program product comprising computer program code for acquiring data relating to properties of a sensor in fluid communication with at least one channel of the microfluidic substrate; and
- a data accessing system for accessing the data relating to properties of the sensor and for providing the data to the first computer program product.
- 143. (Original) The system according to claim 142, wherein the system further comprises a microfluidic substrate operably linked thereto and wherein in response to data provided to the first computer program product, instructions from the first computer program product are executed, changing one or more parameters of one or more functions of the microfluidic substrate.
- 144. (Currently Amended) The system according to claim 142, wherein the one or more functions of the microfluidic substrate comprise scanning a <u>cell based biosensor</u> relative to an outlet of at least one microchannel in the substrate by moving the <u>biosensor</u>, moving the substrate, moving both the <u>biosensor</u> and the substrate, and or varying pressure at one or more microchannels of the substrate.

## 145. (Currently Amended) A method, comprising

providing a <u>bio</u>sensor in fluid communication with at least one microchannel of a microfluidic substrate;

providing data to a computer program product for according to any of claims 1-3, wherein in response to the data provided, the computer program product provides instructions to a scanning mechanism to execute one or more scanning functions such that the substrate, the sensor, or the substrate and the sensor move relative to one another, and/or such that pressure is altered in at least one microchannel of the substrate.

146. (Currently Amended) The method of claim 145, wherein an outlet of at least one microchannel of the substrate delivers a fluid stream which contacts the biosensor.

- 147. (Currently Amended) The method according to claim 146, wherein the substrate comprises a plurality of microchannels with outlets opening into a sensor chamber containing the <u>bio</u>sensor and wherein the <u>bio</u>sensor is exposed to a plurality of fluid streams in a sequence.
- 148. (Original) The method according to claim 147, wherein the sequence is preprogrammed.
- 149. (Original) The method according to claim 145, wherein scanning is continuous.
- 150. (Original) The method according to claim 145, wherein the sensor is paused at one or more channel outlets during a selected time interval.
- 151. (Original) The method according to claim 145, wherein at least one of the fluid streams comprises an agent.
- 152. (Currently Amended) The method according to claim 145, wherein the fluid streams provide interdigitating fluid streams of agent and buffer and the sensor is sequentially scanned across the fluid streams.
- 153. (Currently Amended) The method according to claim 145, wherein the <u>bio</u>sensor is stationary and scanning occurs by varying pressure across one or more channel in proximity to the <u>bio</u>sensor.
- 154. (Currently Amended) The method according to claim 147, wherein the sequence is selected based on a response of the <u>bio</u>sensor.
- 155. (Currently Amended) The method of claim 146, wherein the method further comprises measuring a response of the <u>bio</u>sensor to one or more fluid streams.
- 156. (Currently Amended) The method of claim 155, wherein the response comprises a change in an electrical property of the <u>bio</u>sensor.
- 157. (Currently Amended) The method of claim 145, wherein the <u>bio</u>sensor is a cell or cell fraction.

- 158. (Original) The method of claim 156, wherein the response is measured by measured by patch clamp.
- 159. (Currently Amended) The method of claim 155, wherein the response is measured after exposure of the <u>bio</u>sensor to an electric field.
- 160. (Currently Amended) The method of claim 145, wherein the method further comprises the step of entering data relating to one or more properties of the substrate into the display of an interface of a user device in communication with the data processing system, and wherein in response to the entering, the <a href="mailto:biosensor">biosensor</a> is scanned across the one or more fluid streams <a href="mailto:and-or pressure">and-or pressure</a> is varied at one or more channels.
- 161. (Previously Presented) A method for executing one or more functions of a microfluidic substrate comprising executing program code of a computer program product according to any of claims 1-3, wherein the computer program product is operably linked to the microfluidic substrate.
- 162. (New) A computer program product comprising:

a computer readable medium having computer readable program code embodied in the medium for causing an application program to execute on a computer, wherein the program product comprises instructions for controlling a fluid delivery control mechanisms, so that the fluid delivery control mechanism;

delivers a cell based biosensor via a fluid through a first microchannel in a micofluidic substrate to a sensor chamber comprising one or more electrodes in communication with the sensor chamber which form a patch clamp system,

applies a negative pressure to a second microchannel so as to position said cell based biosensor in electrical communication with the one or more electrodes, and

sequentially exposes the cell based biosensor to a plurality of fluid streams from one or more microchannels.

163. (New) The computer program product of claim 162, further comprising computer program code for acquiring data from a detector which detects a property of the cell based biosensor which is in electrical communication with the one or more electrodes.

- 164. (New) A system comprising:

  a first computer program product according to claim 162; and
  a second computer program product comprising computer program code
  for acquiring data from a data acquisition system which detects a property of the
  cell based biosensor which is in contact with the opening of the second
  microchannel.
- 165. (New) The system of claim 164, further comprising a data acquisition system wherein the data acquisition system is operably linked to a microfluidic substrate.
- 166. (New) The system of claim 165, wherein the microfluidc substrate comprises a first microchannel in communication with a sensor chamber comprising one or more electrodes.
- 167. (New) The system of claim 166, wherein said microfluidic substrate comprises an in-chip patch clamp device.
- 168. (New) The system of claim 164, wherein the system provides data to a processor in communication with the substrate to alter one or more substrate functions.
- 169. (New) The system of claim 168, wherein the data processing system accesses data from one or more computer program products, and wherein the data relates to properties or functions of the microfluidic substrate and/or properties of the cell based biosensor in contact with the opening of the second microchannel.

- 170. (New) The system of claim 165, wherein the microfluidic substrate comprises at least one electrically conducting surface for delivering an electric field to the biosensor at the opening of the second channel.
- 171. (New) The system of claim 170, wherein the system further comprises a computer program product for patch clamp data acquisition and analysis.
- 172. (New) The system of claim 170, wherein the electric field is of a strength sufficient to electroporate a membrane of the cell based biosensor.
- 173. (New) The system of claim 165, wherein the computer program product comprises a computer readable program code for causing a computer to input data relating to electric field properties and/or a response or reaction of the biosensor to an agent.
- 174. (New) The system of claim 173, further comprising a detector for detecting a reaction or response of the cell based biosensor.
- 175. (New) The system of claim 174, wherein the data acquisition system receives input data from the detector relating to the reaction or response.
- 176. (New) The system of claim 175, wherein the reaction or response is selected from the group consisting of: a physiological response, a change in calcium levels, hybridization, binding, change in electrical properties, introduction of an agent into and/or onto a cell, introduction of an agent into an intracellular compartment, and combinations thereof.
- 177. (New) The system of claim 176, wherein the reaction or response is a change in electrical properties of the cell based biosensor.
- 178. (New) The system of claim 170, wherein the cell based biosensor is exposed to an electric field.
- 179. (New) The system of claim 178, wherein the data acquisition system receives input data relating to properties of the electric field.

- 180. (New) The system of claim 179, wherein the data acquisition system provides output data to a processor in communication with a power supply for generating the electric field.
- 181. (New) The system of claim 165, wherein the system further comprises a fluid delivery mechanism for controlling delivery of fluid through at least one channel of the substrate and wherein the computer program code further comprises instructions for execution by a processor in communication with the fluid delivery control mechanism to control delivery of fluid.
- 182. (New) The system of claim 181, wherein the instructions comprise instructions to deliver a plurality of agents to one or more channels of the substrate.
- 183. (New) The system of claim 182, wherein the instructions comprise instructions to deliver a plurality of agents from a plurality of sample reservoirs to the cell based biosensor.
- 184. (New) The system of claim 181, wherein the fluid delivery control mechanism applies positive and negative pressure to the microchannels.
- 185. (New) The system of claim 181, wherein the fluid delivery control mechanism applies a positive pressure to the first microchannel and a negative pressure to the second microchannel.
- 186. (New) The system of claim 183, wherein the cell based biosensor is sequentially exposed to multiple fluid steams by varying the pressure in one or more microchannels.
- 187. (New) The system of claim 181, wherein the microfluidic chip contains sample and buffer reservoirs in communication with sample and buffer microchannels which are in communication with the first microchannel which is in communication with a waste microchannel.

188. (New) The system of claim 187, wherein the fluid delivery mechanism applies a positive pressure to sample and buffer channels and a negative pressure to the waste microchannel.

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189. (New) The system of claim 181, wherein the fluid delivery mechanism delivers two or more substantially separate fluid streams through the first microchannel.